IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application Number	:	09/938,669	Confirmation No.:	2508
Applicant	:	Jens PETERSEN		
Filed	:	August 27, 2001		
Title	:	POLYACRYLAMIDE HYDROGEL AS A SOFT TISSUE FILLER ENDOPROSTHESIS		
TC/Art Unit	:	1615		
Examiner:	:	Carlos A. Azpuru		
Docket No.	:	60117.000004		
Customer No.	:	**21967**		

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
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STATEMENT OF SUBSTANCE OF INTERVIEW UNDER 37 C.F.R. § 1.133 AND SUPPLEMENTAL RESPONSE UNDER 37 C.F.R. § 1.111

Sir:

This Supplemental Response is filed in view of the Examiner interview held on February 23, 2006 for the above-referenced application ("the Application") and supplements the Amendment Under 37 C.F.R. §1.111, filed January 9, 2006 ("the Amendment"), responsive to the non-final Office Action of October 7, 2005.

Amendments to the claims are reflected in the listing of claims which begins on page 2 of this Amendment.

Remarks begin on page 8 of this Amendment.

AMENDMENT

This listing of claims will replace all prior versions and listings of claims in the Application. Please amend the claims as follows:

Listing of Claims:

1.-26. (Canceled)

27. (Currently amended) A prosthetic device for soft tissue augmentation consisting essentially of a polymer hydrogel, said polymer hydrogel comprising less than 50 ppm monomeric units, water or an aqueous solution and at least 0.5% by weight polyacrylamide and less than 3.5% by weight polyacrylamide, based on the total weight of the polymer hydrogel, wherein said prosthetic device has a complex viscosity of about 2 to 100 Pas, wherein said polyacrylamide has ~~is defined as having~~ a backbone ~~comprised predominantly~~ consisting essentially of the formula $(C_3H_5NO)_x$, wherein said polyacrylamide is made by a method comprising combining acrylamide and methylene bis-acrylamide and wherein the device is injectable into soft tissue.

28. (Previously presented) The prosthetic device according to claim 27, wherein the polymer hydrogel comprises at least 0.5% by weight polyacrylamide, based on the total weight of the polymer hydrogel.

29. (Currently amended) The prosthetic device according to claim 27, wherein the polymer hydrogel comprises ~~comprising~~ about 1.9 to 2.9% by weight polyacrylamide, based on the total weight of the polymer hydrogel.

30. (Previously presented) The prosthetic device according claim 27, wherein the polymer hydrogel comprises at least 95% by weight water or an aqueous solution based on the total weight of the hydrogel.

31. (Currently amended) The prosthetic device according to claim 27, wherein the polymer hydrogel further ~~comprising~~ comprises cells for cellular engraftment to the surrounding tissue.

32. (Previously presented) The prosthetic device according to claim 31, wherein the cells are stem cells.

33. (Previously presented) The prosthetic device according to claim 27, wherein the polymer hydrogel comprises at least 1.5% by weight polyacrylamide, based on the total weight of the polymer hydrogel.

34. (Canceled)

35. (Currently amended) The prosthetic device according to claim 27 for at least one of cosmetic surgery of the face, ~~or~~ reconstructive surgery of the face, body contouring, ~~or~~ augmentation of the lips or reconstructive surgery of the lips.

36. (Previously presented) The prosthetic device according to claim 35 for cosmetic or reconstructive surgery of the face having a complex viscosity of about 2 to 20 Pas.

37. (Previously presented) The prosthetic device according to claim 35 for body contouring having a complex viscosity of about 5 to 50 Pas.

38. (Previously presented) The prosthetic device according to claim 35 for augmentation or reconstructive surgery of the lips having a complex viscosity of about 2 to 10 Pas.

39. (Previously presented) The prosthetic device according to claim 27 for use in correction of facial contour deformities due to at least one of aging, acne, trauma, surgery, infection or congenital deformities.

40. (Currently amended) The prosthetic device according to claim 39 wherein the correction of facial contour deformities is selected from the group consisting of at least one of a correction of the cheekbones, a correction of nasolabial folds, a correction of glabellar frowns, a correction of depressed contours of the mouth. a correction to the chin, a correction to size of the lips, ~~or~~ a correction to shape of the lips, and a correction to other soft tissue deficiencies of the face.

41. (Previously presented) The prosthetic device of claim 27 wherein the water is pyrogen-free.

42. (Previously presented) The prosthetic device of claim 30 wherein the water is pyrogen-free.

43. (Canceled)

44. (Previously presented) The prosthetic device of claim 27 wherein the polymer hydrogel comprises less than 40 ppm monomeric units.

45. (Previously presented) The prosthetic device of claim 27 wherein the polymer hydrogel has an elasticity module of not less than 10 Pa.

46. (Previously presented) The prosthetic device of claim 27 wherein the polymer hydrogel has an elasticity module of about 10 to 700 Pa.

47. (Previously presented) The prosthetic device of claim 27 wherein the polymer hydrogel has an elasticity module of about 35 to 480 Pa.

48. (Previously presented) The prosthetic device of claim 27 wherein the polymer hydrogel comprises less than 20 ppm monomeric units.

49. (Currently amended) The prosthetic device according to claim 27, wherein said polyacrylamide is made by a method further comprising washing ~~after polymerization~~ with pyrogen-free water or an aqueous solution after the combining of acrylamide and methylene bis-acrylamide.

50. (Previously presented) The prosthetic device according to claim 27, wherein said prosthetic device is in a syringe.

51. (Previously presented) The prosthetic device according to claim 50, wherein said syringe has a volume selected from the group consisting of 0.5 mL, 0.7 mL, 1.0 ml, 1.5 mL, 2.0 mL, 2.5 mL, 5.0 mL, 7.5 mL, 10 mL, 12.5 mL, 15 mL, 20 mL, and 25 mL.

52. (New) A method for soft tissue augmentation comprising administering to an area in need thereof a prosthetic device consisting essentially of a polymer hydrogel, said polymer

hydrogel comprising less than 50 ppm monomeric units, water or an aqueous solution and at least 0.5% by weight polyacrylamide and less than 3.5% by weight polyacrylamide, based on the total weight of the polymer hydrogel, wherein said prosthetic device has a complex viscosity of about 2 to 100 Pas, wherein said polyacrylamide has a backbone consisting essentially of the formula $(C_3H_5NO)_x$, wherein said polyacrylamide is made by a method comprising combining acrylamide and methylene bis-acrylamide and wherein the device is injectable into the soft tissue.

53. (New) The method according to claim 52, wherein the polymer hydrogel comprises at least 0.5% by weight polyacrylamide, based on the total weight of the polymer hydrogel.

54. (New) The method according to claim 52, wherein the polymer hydrogel comprises about 1.9 to 2.9% by weight polyacrylamide, based on the total weight of the polymer hydrogel.

55. (New) The method according to claim 52, wherein the polymer hydrogel comprises at least 95% by weight water or an aqueous solution based on the total weight of the hydrogel.

56. (New) The method according to claim 52, wherein the polymer hydrogel further comprises cells for cellular engraftment to the surrounding tissue.

57. (New) The method according to claim 56, wherein the cells are stem cells.

58. (New) The method according to claim 52, wherein the polymer hydrogel comprises at least 1.5% by weight polyacrylamide, based on the total weight of the polymer hydrogel.

59. (New) The method according to claim 52, wherein the soft tissue augmentation is selected from the group consisting of at least one of cosmetic surgery of the face, reconstructive surgery of the face, body contouring, augmentation of the lips and reconstructive surgery of the lips.

60. (New) The method according to claim 59, wherein the soft tissue augmentation is cosmetic or reconstructive surgery of the face and wherein the prosthetic device has a complex viscosity of about 2 to 20 Pas.

61. (New) The method according to claim 59, wherein the soft tissue augmentation is body contouring and the prosthetic device has a complex viscosity of about 5 to 50 Pas.

62. (New) The method according to claim 59, wherein the soft tissue augmentation is augmentation or reconstructive surgery of the lips and the prosthetic device has a complex viscosity of about 2 to 10 Pas.

63. (New) The method according to claim 52, wherein the soft tissue augmentation is correction of facial contour deformities due to at least one of aging, acne, trauma, surgery, infection or congenital deformities.

64. (New) The method according to claim 63, wherein the correction of facial contour deformities is selected from the group consisting of at least one of a correction of the cheekbones, a correction of nasolabial folds, a correction of glabellar frowns, a correction of depressed contours of the mouth, a correction to the chin, a correction to size of the lips, a correction to shape of the lips, and a correction to other soft tissue deficiencies of the face.

65. (New) The method according to claim 52, wherein the water is pyrogen-free.

66. (New) The method according to claim 55, wherein the water is pyrogen-free.

67. (New) The method according to claim 52, wherein the polymer hydrogel comprises less than 40 ppm monomeric units.

68. (New) The method according to claim 52, wherein the polymer hydrogel has an elasticity module of not less than 10 Pa.

69. (New) The method according to claim 52, wherein the polymer hydrogel has an elasticity module of about 10 to 700 Pa.

70. (New) The method according to claim 52, wherein the polymer hydrogel has an elasticity module of about 35 to 480 Pa.

71. (New) The method according to claim 52, wherein the polymer hydrogel comprises less than 20 ppm monomeric units.

72. (New) The method according to claim 52, wherein said polyacrylamide is made by a method further comprising washing with pyrogen-free water or an aqueous solution after the combining of acrylamide and methylene bis-acrylamide.

73. (New) The method according to claim 52, wherein said prosthetic device is in a syringe.

74. (New) The method according to claim 73, wherein said syringe has a volume selected from the group consisting of 0.5 mL, 0.7 mL, 1.0 ml, 1.5 mL, 2.0 mL, 2.5 mL, 5.0 mL, 7.5 mL, 10 mL, 12.5 mL, 15 mL, 20 mL, and 25 mL.

REMARKS

I. Statement

A personal Examiner interview was held on February 23, 2006. The interview was attended by Examiner Carlos A. Azpuru and Applicant's representatives, Pierre Kary, Ph.D., Stanislaus Aksman and Victoria A. Silcott. Applicant thanks Examiner Azpuru for his time and attention.

Currently pending independent claim 27 was discussed in view of Russian Patent No. RU 2127129, in the name of Lopatin *et al.* ("the '129 patent"), European Patent No. EP 0727232, issued to Brunstedt *et al.* ("the '232 patent") and British Patent No. GB 2114578, issued to Gashinsky *et al.* ("the '578 patent").

First, Applicant's representatives explained that the '129 patent discloses a two-step copolymerization of acrylamide and acrylic acid. They described that when the polymerization of acrylamide is done in alkaline aqueous medium, as is the case in the process disclosed in the '129 patent (*see e.g.*, Translation, page 2, paragraph 5), hydrolysis of the amide occurs, thereby providing carboxylate (when carried out in water, or an ester thereof when carried out in alcohol). This is supported by the first full paragraph on page 49 of the Polymeric Material Encyclopedia (Joseph C. Salamone ed., CRC Press, Inc. 1996), which was shown to the Examiner at the interview and was attached as Appendix A to the Amendment Under 37 C.F.R. §1.111, filed January 9, 2006. Applicant's representatives explained the resulting reactions as depicted in Figure 2 of Appendix A: the hydrolysis of acrylamide to acrylic acid (or ester) (II), the polymerization of the acid (or ester) to the amide (III), and the hydrolysis of the amide in the polymer chain to the carboxylate (or an ester thereof) (IV). Applicant's representatives concluded that the content of the carboxylate subunits ("y" in Figure 2) is quite significant, and, therefore, the backbone of the polyacrylamide would not consist essentially of the formula $(C_3H_5NO)_x$, as claimed by Applicants. Thus, they asserted that the copolymer of acrylamide and acrylic acid disclosed in the '129 patent does not anticipate the claimed polyacrylamide.

Moreover, the Applicant's representatives stated that the '129 patent teaches away from the claimed invention. For instance, they pointed out that the '129 patent states, "the proposed method permits to decrease the amount of unlinked amino groups (NH_2 radicals) in the polymer . . . in the polymer structure the content of NH_2 radicals is less than 1% of the functional groups total amount." *See* Translation, the paragraph spanning from page 3 to page 4. In

addition, they indicated where the '129 patent also states that a known polyacryl amide gel, as taught in International Application Publication No. WO 81/01290, consisting of acrylamide and methylene bis-acrylamide dissolved in physiological solution polymerized in the presence of polymerization initiators and conducted in one operation "is *not* suitable for use as a soft tissue plastics material, since due to the one-step polymerization process it comprises free NH_2 radical . . ." *See* Translation, page 4, third full paragraph to fifth full paragraph (emphasis added). Thus, Applicant's representatives submitted that the claimed invention is also not obvious in view of the '129 patent.

Second, Applicant's representatives differentiated the filling material for an implantable prosthesis as disclosed in the '232 patent from the prosthetic device of the current application. They explained that the filling material, alone, does not provide the properties needed for a prosthetic device because the '232 patent states that the shell must be a viscoelastic membrane. *See* col. 4, ll. 54-57. Moreover, the '232 patent teaches away from using the filling material alone because "the shell must be capable of retaining the filling material without substantial leakage or bleeding." Col. 4, ll. 49-51. Furthermore, if the filling material should leak, it must be relatively easily excretable or metabolized in the body with no adverse effects. *See e.g.*, col. 3, ll. 45-47. Therefore, the filling material could not be used as a prosthetic device as claimed in present application.

Third, Applicant's representatives distinguished the '578 patent from the claimed invention. They explained that the '578 patent discloses a dense base growth medium, artificial crystalline lenses and contact lenses, which "assume[s] the shape and size" of the container used to carry out the polymerization reaction. *See* Translation page 3, fourth full paragraph. Therefore, the polyacrylamide gel described in the '578 patent is likely to be a solid and could not have the complex viscosity of about 2 to 100 Pas nor the ability to be injectable as claimed in the Application.

Fourth, Applicant's representatives brought to the Examiner's attention U.S. Reissued Patent No. RE38,913 ("the Reissued '913 patent"), issued to Pavlyk and submitted in an Information Disclosure Statement on February 13, 2006, since it is now owned by the Assignee of the present application. Applicant's representatives also pointed out to the Examiner that the Reissued '913 patent teaches away from the claimed invention because it states, "Concentrations [of cross-linked polyacrylamide] below 3.5% make the hydrogel unstable." Col. 3, l. 50.

In view of the aforementioned arguments, Examiner Azpuru agreed that the claims appeared to be in condition for allowance.

Finally, Applicant's representatives asked the Examiner if claims directed to the method for soft tissue augmentation comprising administering the claimed prosthetic device could be added to the application. The Examiner agreed to accept the additional claims and to examine them if they included all of the limitations of the claimed prosthetic device.

II. Amendment

Reconsideration of rejections in the Application is respectfully requested. Upon entry of the foregoing amendment, claims 27-42, and 44-74 will be pending. Claims 27-30, 33-42 and 44-48 stand rejected. Claims 31 and 32 are objected to. Claims 27, 29, 31, 35, 40 and 49 are amended. New claims 52-74 are added.

Applicant respectfully requests entry of the above amendment, as discussed during the Examiner interview, and submits that the amendment does not introduce new matter. Support for the amendment to the claims and for new claims can be found throughout the specification (considered as a whole) and in the claims as originally filed. In particular, support for the amendment to claim 27 can be found, *inter alia*, in the specification at page 5, lines 20-23 and page 9, Figure 1. Claims 29, 31 and 49 have been amended to provide terminology consistent with claim 27. Claims 35 and 40 have been amended to clarify the Markush groups. As discussed in the Examiner interview, new claims 52-74 are directed to a method for soft tissue augmentation and include the limitations of claims 27-42 and 44-51 respectively. Support for a method for soft tissue augmentation can be found, *inter alia*, in the specification at page 7, lines 31-34.

Based on the above amendments, the interview, the Amendment and the remarks in this Supplemental Response, Applicant respectfully requests that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

III. Consideration of References

A copy of the Form PTO-1449 submitted on June 20, 2005 with the Request for Continued Examination ("the Form") was not returned with the Examiner's initials in the left column. Therefore, Applicant resubmits, herewith, a copy of the Form and respectfully requests the Examiner to consider the references cited therein and to return a copy of the Form with the

Examiner's initials in the left column in accordance with M.P.E.P. § 609 to indicate on the record that the references were considered.

CONCLUSION

For at least the reasons stated above, claims 27-42, 44-74 are in condition for allowance. Accordingly, Applicant respectfully requests that the Application be allowed and passed to issue.

In the event any outstanding issues remain, Applicant would appreciate the courtesy of a telephone call to Applicant's undersigned representative to resolve such issues in an expeditious manner.

It is believed that no fees are due in connection with this Supplemental Response. However, in the event it is determined by the U.S. Patent and Trademark Office that fees are due, including any fees for a petition for extension(s) of time, the Commissioner is hereby authorized to charge such fees to the undersigned's Deposit Account No. 50-0206.

Respectfully submitted,

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Date: March 10, 2010

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